IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

FOREST LABORATORIES, LLC, FOREST LABORATORIES HOLDINGS, LTD., MERCK KGaA and MERCK PATENT GESELLSCHAFT MIT BESCHRÄNKTER HAFTUNG,	)	
Plaintiffs,	)	
	)	C.A. No. 15-272 (GMS)
v.	)	CONSOLIDATED
ACCORD HEALTHCARE INC.,	)	
Defendant.	)	

PLAINTIFFS' OPENING CLAIM CONSTRUCTION BRIEF

MORRIS, NICHOLS, ARSHT & TUNNELL LLP

Jack B. Blumenfeld (#1014)
Maryellen Noreika (#3208)
1201 North Market Street
P.O. Box 1347
Wilmington, DE 19899
(302) 658-9200
jblumenfeld@mnat.com
mnoreika@mnat.com

Attorneys for Plaintiffs Forest Laboratories, LLC, Forest Laboratories Holdings, Ltd., Merck KGaA, and Merck Patent GmbH

OF COUNSEL:

David B. Bassett
David A. Manspeizer
WILMER CUTLER PICKERING HALE AND DORR LLP
7 World Trade Center
250 Greenwich Street
New York, NY 10007
(212) 230-8800

Vinita Ferrera
Emily R. Whelan
Anna E. Lumelsky
Deric Geng
Will Kinder
WILMER CUTLER PICKERING HALE AND DORR LLP
60 State Street
Boston, MA 02109
(617) 526-6000

June 22, 2016

TABLE OF CONTENTS

TABLE OF AUTHORITIES

Page(s)

Cases

I. INTRODUCTION

Plaintiffs Forest Laboratories, LLC and Forest Laboratories Holdings, Ltd. (collectively, "Forest") market and sell VIIBRYD®, an FDA-approved antidepressant with a novel mechanism of action. Forest is the exclusive licensee of U.S. Patent Nos. 7,834,020 ("the '020 patent"); 8,193,195 ("the '195 patent"); 8,236,804 ("the '804 patent"); and 8,673,921 ("the '921 patent") (collectively, "the patents-in-suit"), which are owned by Plaintiffs Merck KGaA and Merck Patent Gesellschaft mit beschränkter Haftung (collectively, "Merck").

The patents-in-suit relate to crystalline forms of the compound vilazodone HCl—the active ingredient in VIIBRYD®—as well as to related pharmaceutical compositions and methods. These newly-developed crystalline forms of vilazodone possess significant advantages over the originally-developed compound, including prolonged shelf life, improved solubility, and stability against heat and humidity. *See, e.g.*, '804 patent, col. 5, ll. 1-18.

Forest and Merck (collectively, "plaintiffs") filed these patent infringement actions after receiving notice that Defendants Accord Healthcare Inc., Alembic Pharmaceuticals, Ltd., Alembic Global Holding SA, Alembic Pharmaceuticals, Inc., Apotex Inc., Apotex Corp., InvaGen Pharmaceuticals, Inc., and Teva Pharmaceuticals USA, Inc. (collectively, "defendants") had filed Abbreviated New Drug Applications seeking approval to manufacture and sell generic versions of VIIBRYD® prior to the expiration of the patents-in-suit.

The parties have agreed on certain claim constructions, but seven disputes relating to claim construction remain: (1) "crystalline"/"crystalline modification"; (2) "exhibits the following XRD data"; (3) "corresponding to"; (4) "characteristic peak"; (5) "effective amount"; (6) "administer"/"administered"/"administering"; and (7) whether certain preamble claim language is limiting. As set forth more fully below, plaintiffs have proposed constructions that are faithful to the disclosures in the patents-in-suit and to the understanding of a person of

ordinary skill in the art ("POSA"). In contrast, defendants propose litigation-inspired constructions that are inconsistent with the intrinsic evidence and divorced from the way those terms are ordinarily used by a POSA.

II. THE INVENTION OF THE PATENTS-IN-SUIT

Approximately one in six adults suffer from depression at some point in their lives. Declaration of Michael Thase, M.D. ("Thase Decl.") ¶ 25. Depression is a serious medical condition that can contribute to or worsen other chronic diseases and increase the risk of morbidity and mortality. *Id.* While various classes of drugs are available to treat depression, no single antidepressant is effective in all patients. *Id.* ¶ 40. Moreover, unwanted side effects, including sexual dysfunction, weight gain, and sleep disruption, are common, and contribute to frequent switching of medication or even discontinuation of treatment. *Id.* ¶¶ 28-29. At the time of the invention disclosed in the patents-in-suit, there remained a need for new antidepressants with a unique mechanism of action and side effect profile. *Id.* ¶¶ 29-31.[1]

VIIBRYD® was approved by the FDA for the treatment of major depressive disorder. Since that time, VIIBRYD® has helped to satisfy the long-felt need for an improved antidepressant by providing an effective treatment for patients, particularly those who do not respond well to the class of drugs known as selective serotonin reuptake inhibitors (SSRIs). Scientists at Merck developed vilazodone to provide a novel dual mechanism of action as ***both*** an SSRI ***and*** 5-HT_{1A} receptor partial agonist. *Id.* ¶¶ 31-32. Clinical studies suggest that vilazodone has an improved side effect profile compared to other antidepressants. *Id.* ¶ 32.

The patents-in-suit disclose novel crystalline forms of vilazodone, related pharmaceuticals compositions, and methods of treating various conditions, including major

[1] The patents-in-suit all claim priority to a June 2001 patent application.

depressive disorder. The specification provides experimental data on a number of the disclosed crystalline forms. *See, e.g.*, '804 patent, Figs. 1-46; col. 21, l. 14 to col. 27, l. 11.[2] The inventors determined that the newly-developed crystalline forms of vilazodone possess advantages over the original vilazodone compound, such as reduced hygroscopicity (that is, reduced ability to absorb moisture from the air), longer shelf life, increased bulk density, constant bioavailability characteristics, and improved compressibility, thermodynamic stability, resistance to sunlight, solubility, flow and handling properties during tableting, color stability, and filtration properties during production. '804 patent, col. 5, ll. 1-18.

III. PERSON OF ORDINARY SKILL IN THE ART[3]

The claims of a patent should be construed as they would be understood by a POSA at the time of the invention. *See Phillips v. AWH Corp.*, 415 F.3d 1303, 1312-13 (Fed. Cir. 2005) (*en banc*). A POSA regarding the subject matter of the patents-in-suit would have at least a bachelor's degree in chemistry, pharmaceutical sciences, or a related discipline, along with several years of experience working in pharmaceutical solid product development and/or solid state chemistry. *See* Declaration of Joel Bernstein, Ph.D. ("Bernstein Decl.") ¶ 18. A POSA also would have knowledge and experience, and/or access to others with knowledge and experience, in treating patients for depression or other conditions identified in the patents-in-suit, and evaluating the effects of such treatment. *Id.*

---

[2] All four of the patents-in-suits share the same specification. Thus, all references to the specification herein are made to the '804 patent as a representative example, and include corresponding cites in the '020, '195, and '921 patents.

[3] Given the Court's familiarity with patent law, plaintiffs have foregone a dedicated "legal background" section in favor of citing relevant case law where appropriate throughout the brief.

Plaintiffs submit herewith declarations from Dr. Joel Bernstein and Dr. Michael Thase. Dr. Bernstein is an expert in solid state chemistry, who has had expertise well beyond the level of a POSA since before the time of the invention, and Dr. Michael Thase is an expert in the diagnosis and treatment of mood disorders, who provides the perspective of a clinician who can advise a POSA regarding medical aspects of the claimed inventions.

IV. THE DISPUTED CLAIM TERMS AND PHRASES

A. "Crystalline" / "Crystalline modification"

Claim Term	Patent/claim	Plaintiffs' Proposed Construction	Defendants' Proposed Construction
"crystalline"	'195 patent, claim 1 '020 patent, claim 1 '921 patent, claims 1, 5, 11, 13 '804 patent, claim 1	Plain meaning/no construction required	Entirely in crystalline form comprising only Form I to XVI, and combinations thereof (as appropriate)
"crystalline modification"	'020 patent, claim 1 '921 patent, claims 1, 5, 11, 13 '804 patent, claim 1	Crystalline form	Construe together with "crystalline"

The parties' key disputes regarding the "crystalline" claim terms are (1) whether the common term "crystalline" requires construction (as defendants argue), or whether the plain meaning of the term should apply; (2) whether the term "crystalline" requires 100% crystalline material (as defendants appear to contend), or whether it allows for a compound that contains a mixture of crystalline and non-crystalline materials; (3) whether the term "crystalline" is limited only to the specific forms expressly exemplified in the patents (as defendants argue) or also includes other crystalline forms; and (4) whether the distinct terms "crystalline" and "crystalline modification" should be construed to have the same meaning (as defendants argue) .

a) ***"Crystalline" does not require construction because it has a well-understood plain meaning to a POSA***

There is a "'heavy presumption' that a claim term carries its ordinary and customary meaning." *CCS Fitness, Inc. v. Brunswick Corp.*, 288 F.3d 1359, 1366 (Fed. Cir. 2002) (citation omitted). "Crystalline" has an ordinary and customary meaning that is well-understood to a POSA: it refers to a solid form in which atoms or molecules are arranged with a three-dimensional long-range order. *See* Bernstein Decl. ¶¶ 19, 35 (citing Bruno Hancock *et al*., J. Pharma. Scis., 1997, vol. 86, at 1; A Dictionary of Chemistry 140 (John Daintith Ed., 3rd ed. 1996)); *cf. Pfizer Inc. v. Dr. Reddy's Labs. Ltd.*, C.A. No. 09-943-LPS, 2011 WL 767849, at *7 (D. Del. Feb. 28, 2011) (Stark, J.) (construing "crystalline" to mean "a solid form having a long range periodic ordered structure extending in three dimensions").

The intrinsic evidence confirms that the inventors intended "crystalline" to have its plain and ordinary meaning. Neither the patent specifications nor the file histories contain a specific definition of "crystalline," but instead simply use the term as it is ordinarily used by POSAs when discussing crystalline forms. *See, e.g.*, '804 patent, Abstract, col. 2, l. 39 to col. 3, l. 30; col. 4, ll. 18-20, 32-38, col. 5, ll. 1-22, col. 8, ll. 12-18, col. 9, ll. 5-8, col. 11, ll. 34-39, col. 12, ll. 5-13, 39-42, 61-67, col. 13, ll. 62-64, col. 16, ll. 10-13; '921 File History, 9/19/2013 Preliminary Amendment at 3-5 and 12/13/2013 Notice of Allowability at 2; *see also* Bernstein Decl. ¶ 36. These uses of "crystalline" are fully consistent with the term's plain meaning to a POSA. *Id.*

Defendants, by contrast, propose construing "crystalline" to ***include the term itself,*** combined with additional language. In doing so, defendants effectively admit that the term "crystalline" itself requires no construction, because it has a plain and ordinary meaning that is understood to skilled artisans. Moreover, the very circularity of defendants' proposed construction requires its rejection, and application of the term's plain meaning. *See, e.g.*,

Genzyme Corp. v. Atrium Med. Corp., 212 F. Supp. 2d 292, 329 n.22 (D. Del. 2002) (Thynge, Magis. J.) ("To construe closing means to mean closing member is a circular definition that is meaningless."); *ACQIS, LLC v. Alcatel-Lucent USA, Inc.*, No. 6:13-CV-638, 2015 WL 1737853, at *4 (E.D. Tex. Apr. 13, 2015)(accepting plaintiff's proposed construction in part to "avoi[d] confusion that could result from Defendants' circular construction"); *Sparton Corp. v. United States*, 68 Fed. Cl. 34, 47 (2005) ("To the extent that Plaintiff's proposed meaning is a circular definition (*i.e.*, one that uses the word that it attempts to define in the definition itself), it is clearly improper.").

b) The claims do not require "entirely crystalline material"

Beyond its circular nature, defendants' proposal that "crystalline" means "entirely in crystalline form" is vague and ambiguous—it is not apparent from their proffered construction whether defendants intend to argue that an infringing product must be "entirely crystalline," or that only the portion of the infringing product that is "crystalline" must be "entirely crystalline." Either way, defendants' proposed construction should be rejected.

To the extent defendants' proposed construction is intended to suggest that an infringing compound or composition must contain only crystalline material, and cannot contain any non-crystalline material, such a transparently litigation-inspired interpretation has no support in the intrinsic record. *See* Bernstein Decl. ¶¶ 35-37. Nothing in the patents-in-suit or the prosecution histories suggests that a compound must be "entirely" crystalline to fall within the claims. *Id.*¶ 37. Moreover, Federal Circuit precedent supports that a claim reciting a compound in a particular crystalline form covers that compound regardless of the amount or surroundings. *See, e.g., SmithKline Beecham Corp. v. Apotex Corp.*, 403 F.3d 1331, 1339, 1341 (Fed. Cir. 2005) (claim reciting "[c]rystalline paroxetine hydrochloride hemihydrate" was infringed because

"Apotex's PHC anhydrate tablets would contain trace amounts of PHC hemihydrate"); *see also, e.g., Takeda Pharm. Co. v. Handa Pharm. LLC*, No. C-11-00840 JCS, 2013 WL 9853725, at *62-63 (N.D. Cal. 2013).

Furthermore, the open-ended term "comprising" in many of the claims indicates that unrecited (and potentially non-crystalline) elements are not excluded by the claims. *See, e.g.*, '921 patent, claim 11 ("A pharmaceutical composition ***comprising*** a compound which is [vilazodone] hydrochloride anhydrate in its crystalline modification IV . . . ") (emphasis added); *Mars Inc. v. H.J. Heinz Co.*, 377 F.3d 1369, 1376 (Fed. Cir. 2004)("comprising" is an "open-ended" claim term). Indeed, in other cases involving patents disclosing polymorphs, this Court and other courts have interpreted "comprising" in precisely this way. *See In re Armodafinil Patent Litig.*, 939 F.Supp.2d 456, 474 (D. Del. 2013) (Sleet, J.) (claims reciting composition "comprising" particular polymorph allows for other active ingredients and other polymorphic forms). Here, defendants ignore the accepted meaning of "comprising" and incorrectly interpret the asserted claims as if they all contained the "closed" phrase "consisting of." *PPG Indus. v. Guardian Indus. Corp.*, 156 F.3d 1351, 1354 (Fed. Cir. 1998). There is no basis for such a reading.

Further, defendants' proposed construction runs afoul of the prohibition against reading additional limitations from the specification into a claim term, unless "the patentee explicitly redefines the term or disavows its full scope." *Thorner v. Sony Comput. Entm't Am., LLC*, 669 F.3d 1362, 1367 (Fed. Cir. 2012). Here, where there is ***no*** support in the specification—or anywhere else in the record—for defendants' proposed "entirely" limitation, such a construction is clearly improper.

Defendants' position is also inconsistent with the understanding of a POSA: a POSA understands that a compound can contain a mixture of crystalline and non-crystalline materials, but the crystalline portion is still present as the crystalline compound, and the mixture can still exhibit crystalline properties. Bernstein Decl. ¶ 37. For example, if an active pharmaceutical ingredient ("API") in a tablet contains both crystalline and non-crystalline materials, X-Ray diffraction analysis of the tablet may still detect peaks characteristic of the crystalline material. *Id.*

Finally, to the extent defendants' proposed construction means that the portion of the infringing product that is crystalline must be "entirely crystalline," that is a tautology, because any amount of crystalline material is by definition entirely crystalline. Just as it would be unhelpful to define "blue" to mean "entirely blue," it makes no sense to define "crystalline" as "entirely in crystalline form." Bernstein Decl. n.2.

c) "Crystalline" is not limited to certain exemplary forms from the specification

Similarly improper is defendants' attempt to limit "crystalline" to "comprising only Forms I to XVI, and combinations thereof (as appropriate)." That proposed requirement departs from the plain meaning of "crystalline"—which has no such limitation—with no basis in the intrinsic or extrinsic evidence. *See* Bernstein Decl. ¶¶ 38-39.

Consistent with the plain meaning of "crystalline," the patent specification uses the term generally and contains no limitation to specific crystalline forms. For example, the specification speaks generally about solvates, hydrates, and anhydrates of vilazodone hydrochloride and dihydrochloride in their "crystalline modifications" and their "use for the treatment and prevention of depressive disorders" and other disorders. '804 patent, col. 2, ll. 39 to col. 3 ll. 19; *see also* col. 11, ll. 34-36; col. 13, ll. 62-64; col. 14, ll. 29-32. The file history uses the term

"crystalline" in a similarly general way. *See, e.g.*, '921 File History, 12/13/2013 Notice of Allowability at 2. Nothing in the intrinsic evidence suggests that "crystalline" should be limited to the particular crystalline forms disclosed in the specification.

Defendants' proposal to limit the claimed invention to the disclosed embodiments is improper. *See Williamson v. Citrix Online, LLC*, 770 F.3d 1371, 1377 (Fed. Cir. 2014) ("This court has repeatedly 'cautioned against limiting the claimed invention to preferred embodiments or specific examples in the specification.'" (citation omitted)). It is also contrary to the clear statement in the specification that "[t]he preferred specific embodiments and examples are . . . to be construed as merely illustrative, and not limitative to the remainder of the disclosure in any way whatsoever." *See, e.g.*, '804 patent, col. 16, ll. 20-22. Indeed, the references to specific forms in the patent specification (*see, e.g.*, '804 patent, col. 2, ll. 33-35) supports plaintiffs' position, given that it demonstrates that the patentees narrowed their focus to specific crystalline forms when describing certain embodiments, but used the term "crystalline" more generally.[4] *See* Bernstein Decl. ¶¶ 38-39.

Finally, the phrase "as appropriate" in defendants' construction is unclear, and the proposed construction is ambiguous as to whether one or all of the specified forms are required by the construction.

d) "Crystalline" and "crystalline modification" are not the same

Lastly, the parties disagree regarding the construction of the term "crystalline modification": while plaintiffs propose that it be construed to mean "crystalline form"

[4] Thus, the reference to Forms I-XVI as "products of the invention" in the patents-in-suit (*see* '804 patent, col. 14, ll. 60-65) does not imply that the claims are limited to these forms, but merely indicates that these are preferred embodiments. *See Brookhill-Wilk 1, LLC v. Intuitive Surgical, Inc.*, 334 F.3d 1294, 1301 (Fed. Cir. 2003) (specification section describing "Objects of the Invention" did not limit claim to the listed objectives).

(incorporating the plain meaning of "crystalline"), defendants assert that "crystalline modification" and "crystalline" should be construed to mean the same thing. Plaintiffs' construction is supported by the applicant's lexicography. *See, e.g.*, '804 patent, col. 2, ll. 36-38 ("Throughout the specification, the term 'Form' is generally used as a synonym for the term 'modification' or 'crystalline modification.'"); *see also* Bernstein Decl. ¶ 40. Defendants' position, by contrast, is contrary to the intrinsic evidence, and is also untenable based on simple grammar—while "crystalline" is an adjective, "crystalline modification" is a noun phrase. The two terms therefore cannot have an identical meaning. *See Braintree Labs., Inc. v. Novel Labs., Inc.*, 749 F.3d 1349, 1355 (Fed. Cir. 2014) ("'There is an inference . . . that two different terms used in a patent have different meanings.'") (citation omitted).

* * * *

In sum, "crystalline" need not be construed because the term has a well-understood meaning to a POSA that is consistent with the intrinsic record. Defendants' proposed construction does not clarify the meaning of the claim term, and improperly reads in limitations that are inconsistent with the intrinsic record, the understanding of a POSA, and well-established principles of claim construction. *See Tris Pharma, Inc. v. Actavis Labs. FL, Inc.*, No. 14-CV-1309, 2016 WL 125495, at *1 n.2 (D. Del. Jan. 8, 2016) (Sleet, J.) (since the parties' constructions do not add clarity, the Court "does not believe a construction more precise than plain and ordinary meaning is required"). Should the Court determine that a construction is required, the term's plain meaning should apply: "a solid form in which atoms or molecules are arranged with a three-dimensional long-range order." Bernstein Decl. ¶¶ 19, 35. Moreover, plaintiffs' proposed construction of "crystalline modification," which is directly supported by the

patent specification and consistent with the understanding of a POSA and basic rules of grammar, should be adopted.

B. "Exhibits the following XRD data"

Claim Term	Patent/claim	Plaintiffs' Proposed Construction	Defendants' Proposed Construction
"exhibits the following XRD data"	'020 patent, claim 1	Displays X-ray diffraction pattern consistent with the following values, with experimental error ranges (*e.g.*, +/- 0.1° for two-theta values)	Must show all the following peaks and intensities

The parties dispute whether "exhibits the following XRD data" requires all of the precise values listed in the claim for peaks and intensities—as defendants argue—or whether standard experimental error ranges apply, as proposed by plaintiffs.

The intrinsic evidence establishes that the claims should be read—consistent with scientific norms—as incorporating experimental error ranges. During prosecution, the applicants stated explicitly that the values in claim 1 of the '020 patent are based on the Table III data in the patent specification. *See* '020 File History, 3/18/2010 Amendment after Non-Final Rejection at 8 ("claim 1 is amended to recite the XRD data for Form IV as set forth at page 41 of the specification," *i.e.*, the Table III data). Table III incorporates an experimental error range, stating that the "XRD instrument is controlled for 2Theta ±0.1°." '020 patent, col. 27, ll. 35-38. Thus, the applicants incorporated experimental error ranges by reference directly from the specification into the claim. Defendants' apparent position that the claims should be interpreted narrowly as

requiring the precise values listed, without accounting for experimental error, is contrary to the intrinsic record, as well as standard scientific practice.[5] Bernstein Decl. ¶¶ 42-44.

Plaintiffs' proposed construction of "exhibits the following XRD data" also is consistent with the understanding of a POSA, who would appreciate that numerical results of scientific experiments ***always*** have error ranges due to, for example, the instrumentation and experimental conditions employed. *Id.* ¶ 25. In particular, a POSA would understand that the exact measured XRD pattern for a particular form can vary due to measurement error, *see id.* ¶¶ 25, 43, as another court in this district has previously concluded. *See Eisai Co. v. Glenmark Pharms., Ltd.*, C.A. No. 13–1279, 2015 WL 1228958, at *8 (D. Del. Mar. 17, 2015) (Stark, J.) (since experts agreed that "XRPD . . . was universally known at the pertinent time [late-1990s] to be subject to measurement error," "[i]t follows that a [POSA's] understanding of the term XRPD would include the expected error associated with the measurement being used"). Thus, a POSA would read claim 1 of the '020 patent to incorporate standard experimental error ranges. *See* Bernstein Decl. ¶¶ 42-44. Defendants' proposed construction ignores this scientific reality without justification.

C. "Corresponding to"

Claim Term	Patent/claim	Plaintiffs' Proposed Construction	Defendants' Proposed Construction
"corresponding to"	'804 patent, claims 1-3	Plain meaning/no construction required	Matching the precise values recited in the claims

[5] The fact that claims of the '804 patent list specific error ranges does not imply that error ranges are therefore inapplicable to the values in claim 1 of the '020 patent. As noted above, the applicants made clear that the error ranges listed in the specification apply to the '020 patent claims. Moreover, excluding error ranges would be contrary to the fundamental scientific principle, well-understood by a POSA, that experimental error always should be considered.

The parties dispute whether "corresponding to" requires a precise match to the numerical values recited in the claims (as defendants assert), or whether the term is clear to a POSA and requires no construction (as plaintiffs argue).

"Corresponding to" is a straightforward term understandable to any POSA: a POSA would know that the phrase simply means "consistent with," and requires no further explication. Bernstein Decl. ¶¶ 46-47. Since the term is clear on its own, no construction is necessary. *See Tris Pharma*, 2016 WL 125495, at *1 n.2.

Defendants' position that "corresponding to" requires a "precise" match to the values recited in the claims suffers from the same defects as their position regarding "exhibits the following XRD data" in the '020 patent. In fact, defendants' interpretation—which appears to exclude any error range—is contradicted by the language of the '804 patent's claims, which expressly recite an experimental error range of ±0.1° for the identified two-theta values. '804 patent, col. 27, l. 14 to col. 28, l. 15. The specification recites the same error range. *See, e.g.*, '804 patent col. 24, ll. 34-35. Further, as with "exhibits the following XRD data," defendants' proposed construction ignores the fact—well-known to a POSA—that the numerical results of repeated scientific experiments are never precisely identical. Bernstein Decl. ¶ 47. Since a POSA would know that claims 1-3 are based on experimental data in the specification, the POSA would understand that "corresponding to" does not require a precise match to the values recited in the claims.

D. "Characteristic peak"

Claim Term	Patent/claim	Plaintiffs' Proposed Construction	Defendants' Proposed Construction
"characteristic peak"	'804 patent, claims 1-3	Peak representative of a crystalline form's X-ray diffraction pattern	A powder XRD peak having intensity ≥ 3*noise, which serves to identify the crystalline modification

The key dispute between the parties with respect to "characteristic peak" relates to defendants' assertion that the term requires "intensity ≥ 3*noise."[6] Both the intrinsic record and extrinsic evidence contradict defendants' position.

Table III in the patent specification lists XRD data for "10 characteristic peaks of each polymorph." '804 patent, col. 24, ll. 32-34. The reference to "10 characteristic peaks" rather than "***the*** 10 characteristic peaks" indicates that there could be additional peaks that are not listed in the table, but that are nevertheless "characteristic." Indeed, the table states that "[f]urther peaks exhibit intensities < 3*noise." '804 patent, col. 27, l. 11. Thus, Table III specifically contemplates additional characteristic peaks with intensity less than 3*noise, contradicting defendants' proposed construction. *See* Bernstein Decl. ¶ 52. Moreover, claims 1, 2 and 3 all include the term "characteristic peak" and all refer to crystalline modification IV, but they do not each list the ***same*** peaks. This fact further confirms that "characteristic peak" is not a term of exclusion, but rather indicates representative peaks for a particular crystalline form.

Defendants' proposed construction is also inconsistent with the understanding of a POSA. A POSA would understand that a "characteristic peak" is simply a peak that can be used to identify a particular crystalline form and distinguish it from other materials. *See* Bernstein

[6] As discussed in more detail below, 3*noise is a statistical measure of confidence level. *See also* Bernstein Decl. ¶ 51.

Decl. ¶ 49. A POSA would know that the intensity of a particular XRD peak is not an absolute property of a crystalline form, but rather one that can vary depending on the particular experimental conditions. *Id.* A POSA therefore would not define a characteristic peak based on a threshold intensity level compared to noise.

Moreover, a POSA would understand that 3*noise is simply a statistical measure of confidence level—3*noise corresponds to a 99% confidence level, while 2*noise corresponds to 90% confidence, and 1*noise to 68% confidence—not a measure of whether a peak can be used to identify a specific crystalline form. *Id.* ¶ 51. In fact, a POSA reliably can identify a specific crystalline form based on peaks with intensities less than 3*noise. *Id.* ¶¶ 50-52. For this reason, it is unreasonable to define "characteristic peak" in the '804 patent claims to require intensity ≥ 3*noise. Instead, a POSA would understand "characteristic peak" in the '804 patent claims to refer to a "peak representative of a crystalline form's X-ray diffraction pattern." *Id.* ¶ 49.

E. "Effective amount"

Claim Term	Patent/claim	Plaintiffs' Proposed Construction	Defendants' Proposed Construction
"effective amount"	'804 patent, claim 1 '195 patent, claims 1-2 '921 patent, claims 13-14	Amount sufficient to promote a therapeutic effect	An amount of the specified crystalline modification of vilazodone HCl sufficient to produce the desired effect

The parties' disagreement regarding the construction of "effective amount" centers on two issues: (1) whether the construction should include the phrase "specified crystalline modification of vilazodone HCl," and (2) whether an effective amount must "produce" rather than just "promote" the relevant effect.

The claim language resolves the first dispute. Each of the claims at issue explicitly identifies what substance must be present in an "effective amount." *See, e.g.,* '804 patent, col. 27, l. 16 to col. 28, l. 1 ("an effective amount ***of*** a compound which is [vilazodone] hydrochloride anhydrate in crystalline modification IV (Form IV)"). Defendants' proposal, which includes "of the specified crystalline modification of vilazodone HCl," is therefore redundant and unnecessary to understand the substance to which the phrase "effective amount" applies. *See U.S. Surgical Corp. v. Ethicon, Inc.*, 103 F.3d 1554, 1568 (Fed. Cir. 1997) (claim construction "is not an obligatory exercise in redundancy"); *Digital-Vending Servs. Int'l, LLC v. Univ. of Phoenix, Inc.*, 672 F.3d 1270, 1275 (Fed. Cir. 2012) (highlighting "the importance of construing claim terms in light of the surrounding claim language").

Claim 1 of the '195 patent further illustrates the flaw in defendants' position. Claim 1 does ***not*** recite an effective amount of a "crystalline modification," but rather an effective amount of "a crystalline hydrochloride salt" of vilazodone. '195 patent, col. 26, ll. 61-63. Defendants' proposed construction thus would import into claim 1 a term—which the parties have asked the Court to construe separately—that is present only in the claims of ***other*** patents.

As to the parties' second dispute, plaintiffs' position that "effective amount" refers to an amount sufficient to ***promote*** a therapeutic effect is consistent with the understanding of a clinician. Clinicians understand that virtually no medicine is effective 100% of the time or in 100% of patients. This is particularly true of antidepressants, which affect different patients differently, and none of which eliminates depression in all patients. Thase Decl. ¶ 40. The Merck inventors who originally developed vilazodone recognized this in the specification for U.S. Patent No. 5,532,241 ("'241 patent"), which is incorporated by reference in the patents-in-

suit. *See* '804 patent, col. 16, ll. 24-26; '241 patent, col. 8, ll. 49-50 ("the particular dose for each individual patient depends on a very wide variety of factors"); Thase Decl. ¶ 43.

Plaintiffs' proposed construction also recognizes that a drug product or treatment regimen may include two or more components, each of which contributes to—or ***promotes***—the desired effect. Thase Decl. ¶ 44; *see also* '804 patent, col. 16, ll. 10-14 ("For the treatment of certain conditions it may be desirable to employ the specific crystalline forms of the present invention in conjunction with another pharmacologically active agent"). In such a therapy, there may be an effective amount of each component even if no component alone is present in an amount sufficient to ***produce*** the desired effect. Thase Decl. ¶ 44.

Defendants' proposed construction of "effective amount," requiring an amount sufficient to ***produce*** the desired effect, is thus inconsistent with the understanding of a POSA. Requiring that a drug achieve its intended effect in all cases ignores clinical reality. *Id.* ¶ 40. Moreover, defendants' construction is inconsistent with the parties' agreed construction of "treating" as "***attempting*** to cause a therapeutic effect on." *See* D.I. 80, Ex. A (emphasis added). That agreed construction makes clear that treatment need not always achieve the desired effect. It follows that a clinician treating a patient with an "effective amount" of a drug does not expect to consistently "produce the desired effect" but only to "promote a therapeutic effect."

"Effective amount" should thus be construed as "an amount sufficient to promote a therapeutic effect," consistent with the intrinsic evidence and the understanding of a POSA.

F. "Administer" / "Administered" / "Administering"

Claim Term	Patent/claim	Plaintiffs' Proposed Construction	Defendants' Proposed Construction
"administer" "administered" "administering"	'020 patent, claim 2 '195 patent, claims 1-2 '804 patent, claim 1 '921 patent, claims 10, 12-14	Plain meaning/no construction required	Deliver[ed/ing] into the body

The parties disagree as to whether the term "administer," and related claim terms "administered" and "administering," require construction. "Administer" is a straightforward term that is ubiquitous and immediately understandable in the field of medicine, including in treating patients for depression, and simply refers to providing a patient a drug or treatment for a therapeutic purpose. Thase Decl. ¶ 48. Unsurprisingly, the intrinsic record is silent on the meaning of this everyday term. Any proper construction of "administer" would simply paraphrase without adding clarity, so the term need not be construed by the Court. *See C.R. Bard, Inc. v. U.S. Surgical Corp.*, 388 F.3d 858, 863 (Fed. Cir 2004) ("[M]erely rephrasing or paraphrasing the plain language of a claim by substituting synonyms does not represent genuine claim construction."); *Tris Pharma*, 2016 WL 125495, at *1 n.2.

Defendants' proposed construction focuses narrowly on inserting the medication into a patient's body. But nothing in the claims or intrinsic evidence limits the claim to physical delivery of the claimed compounds or compositions into the body. For example, a clinician would not understand "administer" to refer solely to the physical act of "delivering into the body" the medication. Rather, while ingesting a medication ***is*** "administering" the medication, "administering" also encompasses a doctor prescribing the medication to the patient. Thase Decl. ¶ 48. Defendants' proposed construction is inconsistent with this ordinary understanding

and should be rejected. *Cf. Shire LLC v. Amneal Pharms., LLC*, No. 11-CV-3781, 2013 WL 4045622, at *17 (D.N.J. Aug. 8, 2013) (rejecting defendant's proposed construction of "administering" as "physically delivering into the body of the patient," and adopting plaintiff's proposal of plain meaning).

Thus, no construction of "administer" is necessary because the plain and ordinary meaning of that term is well understood to a POSA.

G. Preamble

Claim Term	Patent/claim	Plaintiffs' Proposed Construction	Defendants' Proposed Construction
"A method of treating a patient suffering from a depressive disorder, an anxiety disorder, a bipolar disorder, mania, dementia, a substance-related disorder, a sexual dysfunction, an eating disorder, obesity, fibromyalgia, a sleeping disorder, a psychiatric disorder, cerebral infarct, tension, side-effects in the treatment of hypertension, a cerebral disorder, chronic pain, acromegaly, hypogonadism, secondary amenorrhea, premenstrual syndrome, undesired puerperal lactation, or combinations thereof"	'020 patent, claim 2 '921 patent, claims 10, 12 -14	Entire preamble is limiting	"A method of treating," is not limiting

The parties agree that substantially all of the preamble in the '020 patent, claim 2, and in the '921 patent, claims 10 and 12-14, is limiting. However, it is defendants' position that the phrase "a method of treating" (alone) in each of these preambles is not limiting.

"In general, a preamble limits the invention if it recites essential structure or steps, or if it is 'necessary to give life, meaning, and vitality' to the claim." *Vizio, Inc. v. Int'l Trade Comm'n*,

605 F.3d 1330, 1340 (Fed. Cir. 2010). In agreeing that the bulk of the disputed preambles are limiting, defendants concede that these preambles "give life, meaning, and vitality" to the claim. The phrase "a method of treatment" in these preambles is as fundamental to understanding the claimed invention as the remainder of the preamble language, because administering the claimed compound would be meaningless without the objective—treatment. *See* Thase Decl. ¶¶ 53-54; *Vizio*, 605 F.3d at 1341 ("for decoding" language in preamble is limiting because invention "would have little meaning without the intended objective of decoding").

Defendants' position that the recitation of "a patient suffering from" particular illnesses is limiting while "a method of treating" is not also ignores the fact that identifying a disease does not in itself explain the purpose of administering medicine. A patient suffering from a disease may be administered medicine for a variety of purposes, such as for prevention, to alleviate selected symptoms of the disease (*e.g.*, pain or insomnia), or for treatment of the disease condition itself. Thase Decl. ¶ 53. The patent specification supports this understanding as it discloses administering the claimed compounds for both treatment and prevention. *See, e.g.*, '804 patent, col. 2, ll. 51-55 (invention provides vilazodone hydrochloride hydrates in crystalline modifications "and their use for the ***treatment and prevention*** of depressive disorders" (emphasis added)). The asserted claims, however, only claim administering the compounds and compositions for treatment purposes. The "method of treating" preamble language is thus critical for identifying the purpose of the claimed method, and should be construed as limiting the claim. Thase Decl. ¶ 55.

V. CONCLUSION

For the foregoing reasons, plaintiffs' proposed constructions should be adopted.

MORRIS, NICHOLS, ARSHT & TUNNELL LLP

/s/ Jack B. Blumenfeld

Jack B. Blumenfeld (#1014)
Maryellen Noreika (#3208)
1201 North Market Street
P.O. Box 1347
Wilmington, DE 19899
(302) 658-9200
jblumenfeld@mnat.com
mnoreika@mnat.com

Attorneys for Plaintiffs Forest Laboratories, LLC, Forest Laboratories Holdings, Ltd., Merck KGaA, and Merck Patent GmbH

OF COUNSEL:

David B. Bassett
David A. Manspeizer
WILMER CUTLER PICKERING HALE AND DORR LLP
7 World Trade Center
250 Greenwich Street
New York, NY 10007
(212) 230-8800

Vinita Ferrera
Emily R. Whelan
Anna E. Lumelsky
Deric Geng
Will Kinder
WILMER CUTLER PICKERING HALE AND DORR LLP
60 State Street
Boston, MA 02109
(617) 526-6000